

- TBO
- 1. A synthetic nucleic acid sequence which encodes α-galactosidase, wherein at least one non-common codon or less-common codon has been replaced by a common codon and wherein the synthetic nucleic acid has one or more of the following properties: it has a continuous stretch of at least 90 codons all of which are common codons; it has a continuous stretch of common codons which comprise at least 33% of the codons of the synthetic nucleic acid sequence; at least 94% or more of the codons in the sequence encoding the protein are common codons and the synthetic nucleic acid sequence encodes a protein of at least about 90 amino acids in length; it is at least 80 base pairs in length.
- 2. The synthetic nucleic acid sequence of claim 1, where the α -galactosidase nucleic acid is inserted into a non-transformed cell.
- 3. The synthetic nucleic acid sequence of claim 1, wherein the number of non-common or less-common codons replaced or remaining is less than 15.
- 4. The synthetic nucleic acid sequence of claim 1, wherein the number of non-common or less-common codons replaced or remaining, taken together, are equal or less then 6% of the codons in the synthetic nucleic acid sequence.
- 5. The synthetic nucleic acid sequence of claim 1, wherein all non-common or less-common codons are replaced with common codons.
- 6. The synthetic nucleic acid sequence of claim 1, wherein at least 96% of the codons in the synthetic nucleic acid sequence are common codons.
- 7. The synthetic nucleic acid sequence of claim 1, wherein at least 98% of the codons in the synthetic nucleic acid sequence are common codons.



- 8. The synthetic nucleic acid sequence of claim 1, wherein all of the codons are replaced with common codons.
 - 9. A vector comprising the synthetic nucleic acid sequence of claim 1.
 - 10. A cell comprising the nucleic acid sequence of claim 1.
- 11. A method of producing α -galactosidase comprising culturing the cell of claim 10 under conditions in which the nucleic acid is expressed.
- 12. A method for preparing a synthetic nucleic acid sequence encoding α -galactosidase which is at least 90 codons in length, comprising:

identifying a non-common codon and a less-common codon in a non-optimized gene sequence which encodes an α-galactosidase protein; and

replacing at least 94% of the non-common and less-common codons with a common codon encoding the same amino acid as the replaced codon.

- 13. The method of claim 12, wherein at least 96% of the non-common and less-common codons are replaced with a common codon encoding the same amino acid as the replaced codon.
- 14. The method of claim 12, wherein at least 98% of the non-common and less-common codons are replaced with a common codon encoding the same amino acid as the replaced codon
- 15. The method of claim 12, wherein the nucleic acid sequence encodes a protein of at least about 105 or more codons in length.
 - 16. A method of providing a subject with α -galactosidase, comprising:

providing a synthetic nucleic acid sequence that can direct the synthesis of an optimized message for α -galactosidase;

introducing the synthetic nucleic acid sequence into the subject; and



allowing the subject to express the α -galactosidase, thereby providing the subject with the α -galactosidase.

- 17. The method of claim 16, wherein the synthetic nucleic acid is introduced into a cell.
- 18. The method of claim 17, wherein the cell can be an autologous, allogeneic, or xenogeneic cell.
- 19. The method of claim 17, wherein the codon optimized synthetic nucleic acid sequence is inserted into the cell *ex vivo* or *in vivo*.
- 20. The method of claim 17, wherein at least 94%, or all of the codons in the synthetic nucleic acid sequence are common codons.
- 21. The method of claim 17, wherein at least 96%, or all of the codons in the synthetic nucleic acid sequence are common codons.
- 22. The method of claim 17, wherein at least 98%, or all of the codons in the synthetic nucleic acid sequence are common codons.
- 23. The method of claim 17, wherein the number of codons which are not common codons is equal to or less than 15.
- 24. The method of claim 17, wherein the subject has a disorder characterized by an α-galactosidase deficiency.
 - 25. The method of claim 24, wherein the subject has Fabry disease.

